Effect of fibrin hydrogel composition on fiber network structure and solute diffusivity

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Introduction

Molecular transport affects local solute concentrations and therefore can be expected to modulate cell behavior in tissue engineering constructs, such as hydrogel-based carriers[1]. In this study we examined the effect of fibrin hydrogel composition, in particular fibrinogen, thrombin and factor XIII concentration on the fiber network structure and the diffusivity of small solutes with a molecular weight similar to that of morphogens. Finally, we explored to what extent differences in diffusivity can be explained from differences in structural properties.

Materials and Methods

Hydrogels with different concentrations of fibrinogen (5, 10 and 20mg/ml), thrombin (0.02 and 0.2U/mg fibrinogen) and factor XIII (0.02 and 2U/mg fibrinogen) were prepared and imaged by confocal fluorescence microscopy. Image stacks were analyzed by means of a fiber extraction algorithm[2] in order to obtain structural information on the fiber network (fiber length, density and diameter). The relative diffusivity (ratio of diffusivity in a hydrogel to the diffusivity in solution, D/D_o) of dextran probes of 10 and 40kDa was measured using Fluorescence Recovery After Photobleaching (FRAP)[3].

Results and Discussion

Image analysis showed that fibrinogen mainly regulates fiber density (fiber length per unit of volume) with values ranging from 0.3 to 1.3 $\mu m/\mu m^3$ for compositions with low amounts of the two enzymes and fibrinogen concentrations of 5 and 20 mg/ml respectively. Relative diffusivity moderately decreased with an increase of fiber density, with relative diffusivity values ranging from 0.76 to 0.90 for 10kDa and from 0.71 to 0.80 for 40kDa dextran. For 10kDa dextran, at 5 mg/ml fibrinogen an increase in thrombin leads to a decrease in diffusivity, while at 20 mg/ml fibrinogen, an increase in factor XIII leads to a decrease in diffusivity. Diffusivity of 40kDa dextran is affected by both enzymes, but the effect (positive or negative) is depending on fibrinogen concentration. In conclusion, modifications of fibrin hydrogel compositions result in large changes in fiber density, but only moderate changes in diffusivity of solutes within the range of 10 to 40kDa.

References

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